



U.S. Pharmacopeia
The Standard of Quality™

November 23, 2010

Janet Woodcock, M.D.
Director, Center for Drug Evaluation and Research
Food and Drug Administration
10903 New Hampshire Avenue
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Dear Dr. Woodcock:

Thank you for your letter dated October 12, 2010 to the United States Pharmacopeial Convention (USP) concerning drug monographs. We share your objective of helping to ensure the quality, purity, strength and consistency of drugs through robust, up-to-date monographs in USP's official compendia, the *United States Pharmacopoeia (USP)* and *National Formulary (NF)*. We appreciate your continued interest in collaborating with us to achieve this goal. USP compendial standards and Food and Drug Administration (FDA) enforcement of those standards are part of the safety net that for over a century has helped to protect the American public. The increasing globalization of the drug supply—combined with potential new threats—has made our partnership even more critical. Your letter accords with our historic partnership in that FDA by law is to inform USP when it finds 'tests or methods of assay' in our official compendia to be insufficient to determine compliance with compendial standards.

We appreciated the Commissioner's remarks at the USP Convention in April 2010 recognizing this and highlighting the need for continued cooperation between FDA and USP in support of up-to-date public standards. We also note that among the resolutions adopted by Convention delegates at that meeting was Resolution 3, which calls on USP to strengthen its relationship with the FDA (<http://www.usp.org/aboutUSP/resolutions.html>). Like you, we have been encouraged by our recent collaborations with FDA on heparin, glycerin, melamine and other topics. However, as your letter acknowledges, these may be just a small fraction of the potential opportunities for strengthening our joint work to protect the American public. They underscore the need for FDA and USP to collaborate more proactively on modernization efforts that can help prevent the occurrence of public health incidents.

We were glad to have the opportunity to discuss your October 12th letter with Ms. Helen Winkle and her staff at our October 26, 2010 quarterly meeting, and appreciated that so many staff from other organizational units in CDER and the agency were able to attend and participate in the discussion. At that meeting, we shared with FDA the extensive analysis USP has conducted to identify all monographs in the *USP-NF* in need of updating. As attendees saw, the list of high priority small molecule and excipient monographs currently posted on our website represents only a portion of the entire list, which totals approximately 700 monographs. We had suggested to Dr. Sharfstein and Ms. Winkle in a letter dated February 23, 2010 that FDA work with USP to identify and prioritize monographs in need of modernization, so we were glad to hear that a task force has been formed within CDER for this purpose. Last week we received from the task force the list of the initial group of high priority monographs identified, and are in the process of analyzing this list. Our recent interactions with FDA and CHPA regarding OTC monographs also have been productive, and again we look forward to the agency's input on OTC monographs in need of revision. Updating OTC monographs was a particular point presented by FDA for Convention consideration and is reflected in the above noted Resolution 3.

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Beyond the very positive initiatives to date, I emphasize that identification and prioritization of out-of-date monographs is only the beginning of our work. The real challenge for USP is in obtaining the information and materials necessary for modernization. As you are aware, USP is largely dependent on industry to provide it with the information and candidate materials needed to create up-to-date standards. Industry often is reluctant to provide this assistance. Even when a submission for a new or revised monograph is received, USP is reliant on the limited comments received from other manufacturers and FDA to ensure that the proposal is satisfactory and accommodates all FDA-approved products. Thus, while we share your sense of urgency, we frequently find ourselves severely constrained in our ability to move forward quickly with modernization efforts.

In light of these challenges, we are hopeful that FDA's interest in collaboration with USP will extend beyond merely identifying monographs in need of modernization, and that FDA will work with us on solutions and approaches for gaining the needed information and candidate materials. As we have seen in the heparin, glycerin and melamine cases, FDA can play a pivotal role in encouraging industry to work with USP to develop the new methods needed to update monographs. In addition, we would like to explore ways that FDA can provide input earlier in the revision process and furnish more complete information that will allow modernization proposals to be finalized more quickly.

We would also like to see additional collaboration between USP and FDA labs on updating monograph methods and tests. USP and CDER have recently established a melamine working group to explore how more specific assay and identification tests and screening methods can be used to detect economically motivated adulteration. The parties have agreed to share the results of their respective lab development efforts to advance this work. We also note that a new CRADA between USP and FDA's Office of Regulatory Affairs (which is pending approval at FDA) has as one of its objectives the development of new methods for monograph modernization. We recognize that FDA's laboratory resources, like USP's, are limited, but believe that by coordinating our efforts, more can be accomplished in a shorter amount of time.

We note that while your letter at the outset emphasizes the importance of drug monographs in protecting public health, it focuses only on the need to modernize existing USP monographs. It makes no mention of the fact that many drug products – including products that have been on the market for many years – are missing monographs entirely, and thus lack any public standard to help assure their quality. We hope that our collaboration with FDA on monograph modernization can be expanded to encompass the problem of missing monographs as well. Taking into account both missing monographs and those needing updating, approximately one-third of the *USP* is deficient—and the same is generally true of the *NF*.

To further our excellent progress to date, I propose that you and I speak together, with involved staff as you wish, to make sure USP hears first hand your ideas for advancing our collective work to protect the American public through sound public documentary and reference material standards.

In closing, I emphasize how much USP appreciates your support of monographs in official compendia of the United States.

Sincerely,



Roger L. Williams, M.D.
Chief Executive Officer